

Vaccine Toes Are the New COVID Toes

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Established Facts

- Pernio-like lesions represent 18% of the dermatologic manifestations of laboratory-confirmed primary infection with COVID-19. They were the most heavily reported manifestations, partly attributable to media interest in the phenomenon.
- Pernio-like lesions are associated with milder COVID-19 infection as opposed to thrombotic or ischemic dermatoses which are associated with intensive care admission and higher morbidity and mortality.
- The proposed mechanism for milder symptomatology centers around interferon-1 which is not only an integral part of antiviral immunity but also associated with increased incidence of pernio-like lesions in genetic conditions that confer an increased production of interferon-1.

Novel Insights

- Reports of pernio-like lesions after COVID-19 vaccination support the theory that their presence represents a robust host immune response against viral components.
- Given the previous media interest in reporting pernio-like lesions with primary COVID-19 infection, it is reasonable to expect overrepresentation of pernio-like lesions with vaccination. Patients are increasingly distrustful of evidence-based medicine and thus “COVID toes” represent an important intersection at which the clinician can capture the patient’s trust by providing education and counseling.
- Understanding of the pathophysiology of COVID-19 and how this can translate to dermatologic manifestations is paramount in the care of patients who are hesitant to receive the vaccine. The modern clinician is now tasked with the unprecedented role of educating patients on the dangers of media-generated health information outside of the proper clinical context.

Keywords

COVID-19 vaccine · Pernio-like lesions

Abstract

Introduction: Pernio-like lesions were reported as dermatologic manifestations of COVID-19 as early as May of 2020. Since mRNA COVID-19 vaccines were introduced in Decem-

ber 2020, 9 reports of vaccine-associated pernio-like lesions have been presented in the medical literature. **Case Presentation:** A male in his 60s developed pernio-like lesions on the bilateral toes approximately 1 week after receiving the second dose of the Pfizer-BioNTech COVID-19 mRNA vaccine. His symptoms resolved in 6 weeks. **Conclusion:** The rising number of reports of pernio-like lesions associated with COVID-19 vaccination underlines the importance of the patho-

physiological state of the vaccinated patient and how it relates to dermatological manifestations. Pernio-like lesions are thought to represent a robust host immune antiviral response related to production of interferon-1 in the setting of primary infection; incidences occurring after vaccination further support this theory. Unfortunately, media-generated reports of such reactions have the potential to inflame distrust and fear of the vaccine among the general public. Given the previous media interest in reporting pernio-like lesions with primary COVID-19 infection, it is reasonable to expect overrepresentation of pernio-like lesions with vaccination. There appears to be a general increase in patient distrust of evidence-based medicine and thus “COVID toes” represent an important intersection at which the clinician can capture the patient’s trust by providing education and counseling.

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Introduction/Literature Review

Reports of pernio-like lesions associated with COVID-19 began to emerge in May of 2020 [1, 2]. These lesions were reported at higher frequencies than other dermatologic manifestations [3–5], but this was likely attributable to both the novelty of the dermatosis and perceived media interest. In one international registry of 716 patients with dermatologic manifestations of COVID-19, pernio-like lesions, which represented 18%, were found to correlate with milder disease [6]. The proposed mechanism alluded to the host immune antiviral response, specifically type I interferons, as a key player. Expression of type I interferons is induced by recognition of viral RNA replication by Toll-like receptors. The antiviral response is then achieved through the Janus kinase-signal transducers and activators of transcription pathway [7]. Impaired production of type I interferons (evidenced by low interferon-alpha and beta production and activity) has been associated with increased severity of COVID-19 infection and persistent blood viral loads [8]. Conversely, interferonopathies, a group of genetic conditions with increased production of type I interferons, can manifest with pernio-like lesions. It is proposed that type I interferons are part of a robust immune response and thus can predispose an individual to developing pernio-like lesions. In contrast, thrombotic and ischemic dermatoses such as retiform purpura were associated with a higher severity of COVID-19 leading to intensive care admission and death [6]. The contrast between these manifestations coupled with the pathophysiology underlying each entity allows for insight into how dermatologic manifestations may predict prognosis and even aid in diagnosis and



Fig. 1. Shiny erythema and swelling of the toes.

management of COVID-19. Nowadays, in what could arguably be called “post-vaccine era COVID,” dermatologic manifestations associated with COVID-19 vaccination offer an even keener understanding of the pathophysiology beyond what was known with primary infection only. Here, we present a case of pernio-like lesions in a patient after receiving two doses of the Pfizer-BioNTech mRNA vaccine.

Case Report

A male in his 60s presented with a violaceous hue to the proximal and lateral nail folds and erythema, stinging, and swelling of the bilateral toes (see Fig. 1) approximately 1 week after receiving the second dose of the Pfizer-BioNTech COVID-19 mRNA vaccine. He reported a history of nail psoriasis but no known medical conditions carrying a predisposition for pernio. Physical exam revealed shiny erythema and edema of the toes. He was thus diagnosed with pernio-like lesions attributed to host viral immune response to the COVID-19 vaccine. The time to complete resolution was around 6 weeks. Of particular interest is that the patient received a third “booster” dose several months later and did not experience pernio-like lesions.

Discussion

As we enter an unprecedented era in medicine hallmarked by patient distrust in evidence-based medicine, it is imperative that the clinician maintain a keen, up-to-

date understanding of the dermatologic manifestations of COVID-19 in order to guide patient counseling and education. Both primary infection with COVID-19 and vaccination against COVID-19 have received widespread, emotionally charged, opinion-laden reactions on social media. These, in turn, have sustained a level of distrust that has affected vaccination rates. In the experience of the authors, skin manifestations, given their photographable (and thus shareable) nature, have come under increased scrutiny and contribute to fear among misinformed patients. The authors emphasize that this could be attributable to regional differences in attitudes toward the vaccine. Pernio-like lesions, or “COVID toes” to the layperson, represent a unique intersection between the pathophysiology of human disease and the patient’s understanding of it through the lens of the media. A well-known component of the art of medicine is the balance between risk and benefit. As the “modern” patient begins to increasingly enter the medical reasoning and decision-making process at a singular point, clinicians must incorporate this way of thinking into education and counseling.

As previously discussed, emergence of pernio-like lesions after vaccination against COVID-19 further supports the theory that it may represent a robust host immune response to viral components of the vaccine. In December 2020, the Food and Drug Administration (FDA) of the USA issued authorization for emergency use of the Pfizer-BioNTech and Moderna COVID-19 vaccines. An international registry of 414 patients with cutaneous reactions to the COVID vaccine was subsequently developed by the American Academy of Dermatology in conjunction with the International League of Dermatological Societies in December 2020. This registry of 414 reported reactions spanned from December 2020 to February 2021. Twenty-one percent of patients reported cutaneous reactions after the first dose only as opposed to 63% after the second dose only; 16% reported reactions to both doses. The registry identified 8 reports of pernio/chilblains. Three of these occurred with the first dose of the Moderna vaccine (1.1%) and no cases were reported with the second dose. Three patients (8.8%) receiving the Pfizer vaccine reported pernio-like lesions with the first dose and 2 patients (5.0%) reported lesions with the second dose [9]. Periungual pernio-like erythema has also been reported as a nail manifestation of COVID-19 [10]. The authors emphasize that patients may present with a nail complaint given involvement of the proximal and lateral nail folds in which pernio-like lesions should be on the differential in the appropriate

clinical context. On August 23, 2021, the FDA granted approval to the Pfizer-BioNTech vaccine. As of November 2021, FDA approval has been granted for booster doses of both the Moderna and Pfizer vaccines for people over the age of 18. As more people become vaccinated, it is important to anticipate and understand the possible cutaneous manifestations.

Equipping patients with the understanding that pernio-like lesions are: (1) associated with a milder disease course and (2) may represent a robust host immune response to the vaccine could help ameliorate resistance to vaccination. Disinformation abounds, and it is the role of the clinician to appropriately inform patients of the risks and benefits of COVID-19 vaccination. Given the media attention that “COVID toes” received with primary infection, it is conceivable that reports of this phenomenon with the vaccine could increase fear and distrust among unvaccinated patients. The authors emphasize that this is speculative and susceptible to regional bias towards vaccination. This case of a male in his 60s developing pernio-like lesions after the second dose of the Pfizer COVID-19 vaccine highlights a “risk” of vaccination that may herald an inherent benefit: robust host immune response. The general population does not often have the medical background to incorporate this information into an informed decision; therefore, it is critical to educate patients on such occurrences and maintain a position within the forefront of information sources for the population at large. As more patients become vaccinated, knowledge of pernio-like lesions as a reaction is important to consider in the differential diagnosis of nail fold and periungual erythema.

Statement of Ethics

Written informed consent was obtained from participants (or their parents/legal guardians/next-of-kin) for publication of the details of their medical case and any accompanying images. Ethical approval was not required for this study in accordance with national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

The case details were reviewed by B. Hodge, B.E. Elewski, and C.R. Daniel. The case report was authored by B. Hodge with editing by B.E. Elewski and C.R. Daniel. The photograph was provided by C.R. Daniel.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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